



# Novel Approaches to Monitoring Adherence to HIV Therapy

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# Outline

- Background
- Cell phones technologies
  - Interactive voice response (IVR)
  - Short message service (SMS)
- Wireless adherence monitoring (Wisepill)
- Next steps and summary

# Background

- Tight link between HIV antiretroviral adherence, viral suppression, and drug resistance
- Virologic rebound occurs quickly; probability of viral rebound = 50% after a two week lapse in adherence (*Parienti, PLoS One, 2008*)
- Current measures detect missed doses several weeks to months after they occur and are unable to direct adherence interventions before virologic failure
- Novel approaches are needed to prevent the development of drug resistance and loss of treatment effectiveness

# Self-reported adherence

- Standard assessment in routine clinical practice
- Moderate correlations to virologic suppression  
(*Simoni, AIDS Behav, 2005*)
- Limitations
  - Inaccurate: Social desirability bias
  - Infrequent data collection: Recall bias

# Interactive voice response (IVR)

- Technology that allows a computer to detect voice and keypad inputs
- Used primarily for phone trees and in social science research
  - Reviews (*Corkrey, Behav Res Methods Instrum Comput, 2002; Shroder, Curr HIV/AIDS Rep, 2009*)
  - Daily alcohol consumption (*Perrine, J Stud Alcohol, 1995*)
  - Daily condom use in a disadvantaged, U.S. HIV-positive adult population (*Barta, AIDS Care, 2007*)

# Short message service (SMS)

- HIV/AIDS programs using SMS as reminders or means for education
  - WelTel Kenya 1: RCT of SMS reminders versus standard care (*Lester, Trials, 2009*)
  - Project M in South Africa
- Available data is for primarily for use with community health workers (*Chang, AIDS Patient Care STDS, 2008; Curioso, BMC, 2007; Abayomi, Afr J Med Sci, 2006*)

# Cell phone data collection

## Advantages

- Potential for remote areas
- Automated and scalable
- Potential for reduced social desirability bias
- Frequent data collection
- IVR useful for illiterate participants
- SMS convenient, popular with youth

## Disadvantages

- Requires cell phones, tech infrastructure, and network availability
- Initial start-up costs plus on-going fees
- Implementation challenges
  - technical understanding
  - shared phones
  - phones powered off/ expired battery
  - participants unavailable

# IVR and SMS pilot in Mbarara

- Objective: Assess feasibility, acceptability of IVR and SMS for self-reported adherence
- Data from a 1-month pilot among caregivers of children on ART in Mbarara, Uganda
- 14 participants used IVR; 6 used SMS
- Up to 3 trainings
- Weekly calls quantifying missed doses in local language
- IVR call cycles: every 20 min up 1 hour up to 3 days
- SMS cycles: daily up to 3 days
- PIN used for confidentiality
- Qualitative interviews

# Results

- 48 IVR call cycles initiated (3.8 per caregiver)
- 6 incomplete cycles- busy, network, no answer, call rejection
- 6 successful IVR calls (median adherence 82%)
- Reasons for unsuccessful calls
  - hung up at PIN (42%)
  - inappropriate response to question (27%)

# Results

- 24 SMS cycles initiated (4 per caregiver)
- 6 successful SMS (median adherence 100%)
- Predictors of successful IVR calls/SMS
  - Assessed age, education, literacy, sex
  - Increasing age OR 0.9 ( $p = 0.16$ )

# Qualitative results

- Typical usage- short personal and business arrangements (incoming and outgoing)
- Used pay-as-you-go for airtime, but no experience with PIN, automated surveys
- Limited understanding of phone usage and expected responses for IVR and SMS

# Qualitative results

*“At first those questions confused me. They would ask you for your year. You would still be trying to respond and the call goes off. Then, they say that we shall try to call you back. Yet, the person who had trained me had repeated for me and told me what to do. It really greatly disturbed me. They were hard.”*

*“Well, for the first time I had forgotten what to do, and when trying to click yes the call went off. They came and trained me again and I learnt that when the call comes and you respond, you don't first erase, because when I would try doing so the call would go off.”*

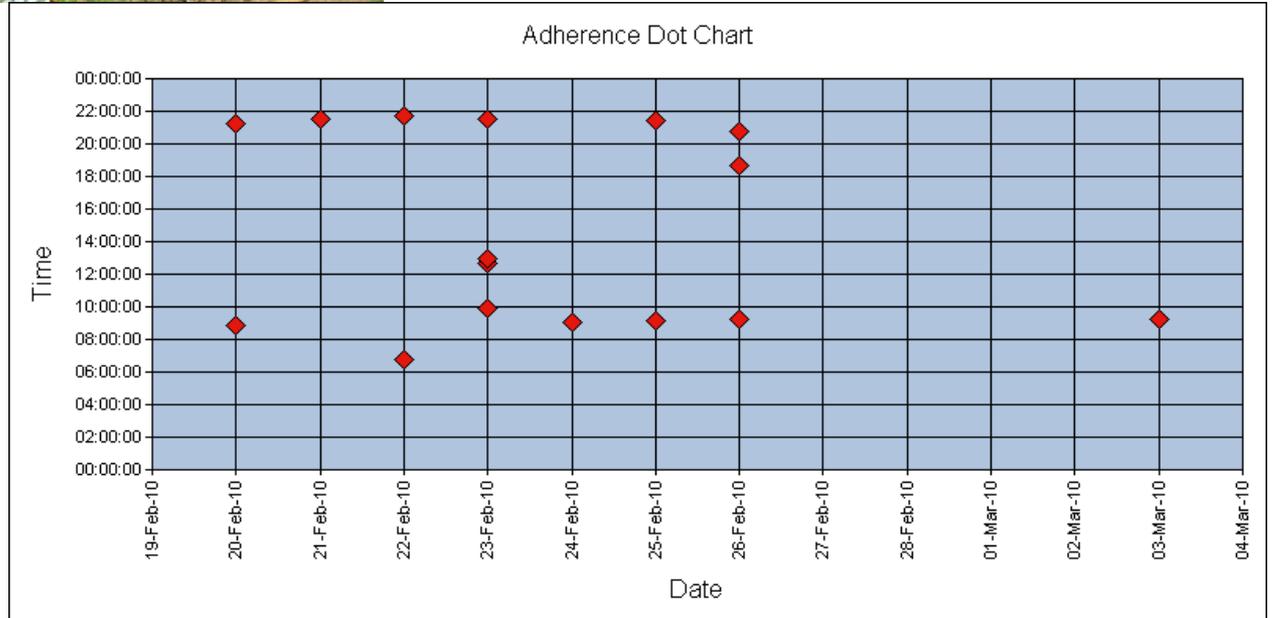
# Qualitative results

- Suggestions for improvement
  - repeated trainings, including groups, over time
  - dedicated cell phone
  - calling from an anticipated number
  - writing down the PIN
  - testing knowledge from the trainings
  - allowing more time for responses

# Wisepill



- Signal sent over cellular network when the device opened
- Daily signal to confirm battery and device functionality
- Flash memory to send signals if travel out of network
- Data transmitted to a server by general packet radio service (GPRS) with back up SMS



# Wireless adherence monitoring

## Advantages

- Real-time data for adherence intervention
- Compatible with blister packs
- Scalable over wide geographic area
- Could allow for strategic viral load monitoring
- Potential for tracking patients lost to follow-up
- Less expensive than viral load and more accurate than CD4 for detecting treatment failure

## Disadvantages

- Limited pill capacity
- Device non-use versus adherence lapse
- Expense (now)
- Limited battery life
- Potential for stigma and/or unintended disclosure

# Wisepill pilot in Mbarara

- Objective: Establish feasibility, acceptability of Wisepill and compare adherence with reference measures
- 10 adult followed prospectively for 2 3-month periods
- Median adherence levels (1<sup>st</sup> 3 months)
  - Prior electronic monitoring: 89%
  - Wisepill: 84%
  - Unannounced pill count: 96%
  - Self-report (3-day and VAS): 100%
- 33 electronically detected interruptions >48 hrs
  - 20 due to battery failure, 7 due to signal transmission problems, 3 unclear (? adherence)

# Wisepill pilot in Mbarara

- After device improvements (2<sup>nd</sup> 3 months)
  - Wisepill: 96%
  - Unannounced pill counts: 99%
  - Self-report (3-day and VAS): 100%
- Continuous data stream with 3 >48 hour interruptions without technical cause
- High acceptability

# Next steps

- Expand the pilots to 500 adults and 100 children
  - Improved IVR/SMS training, including nominal airtime incentive
  - Automated, scaled data management for Wisepill and cell phone data collection
- Link Wisepill data with IVR/SMS and OpenMRS clinical data
- Explore real-time interventions
- Conduct a randomized controlled trial of real-time adherence monitoring as an intervention to prevent viral failure

# Summary

- Real-time adherence monitoring has the potential to prolong treatment success
- Self-reported data collection through IVR/SMS is feasible in resource limited settings, although there are significant challenges to deployment at the patient level
- Wireless adherence monitoring with Wisepill is also feasible and has great potential for adherence monitoring and support

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